REMARKS

Claims Amendments

Claims 1 and 16-18 are pending herein. Claim 3-5 have been withdrawn herein. Claims 1, 3-5 and 16-18 have been amended herein to recite a modified CpG-containing oligonucleotide wherein all CpG dinucleotides present in the oligonucleotide are modified. Support for this amendment can be found throughout the specification, for example, at page 8 lines 8-9. No new matter has been added.

Election/Restriction

Applicants acknowledge the withdrawal of the Restriction Requirement as it applies to Groups I and III and the finality of the rejection as it applies to Groups II and I/III (now rejoined).

Rejoinder

It is Applicants belief that Claims 1 and 16-18 are in condition for allowance and, therefore, respectfully request that withdrawn Claims 3-5 be rejoined.

Rejection of Claims 16-18 Under 35 U.S.C. §112, First Paragraph

Claims 16-18 are rejected under 35 U.S.C. §112, first paragraph, because while the specification is recognized as enabling for methods of reducing the side effects of antisense phosphorothioates having one CpG dinucleotide by modifying the CpG dinucleotide, does not reasonably provide enablement for methods of reducing the side effects of antisense phosphorothioates having multiple CpG dinucleotide by modifying only one CpG.

Claims 16-18 have been amended here to recite a modified CpG-containing oligonucleotide wherein all CpG dinucleotides present in the oligonucleotide are modified. This amendment is clearly supported by the specification. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 1 and 16-18 Under 35 U.S.C. §103(a)

Claims 1 and 16-18 are rejected under 35 U.S.C. §103(a), as being unpatentable over Cook et al. (U.S. Patent Number 5,212,295); Cook et al. (U.S. Patent Number 5,670,633) and Metelev et al. (U.S. Patent Number 6,143,881).

Applicants respectfully disagree. This rejection is far afield from the standards for analysis required by 35 U.S.C. §103, and as interpreted by the Supreme Court in *Graham v. John Deere of Kansas City*, 148 U.S.P.Q. 459 (1966). In particular, the presently maintained rejection ignores the admonition that an obviousness determination much consider "the claimed invention as a whole". *Application of Aufhauser*, 158 U.S.P.Q. 351, 352 (C.C.P.A. 1968). Thus, mere identification of limitations of the claimed invention from disparate references to declare the combination to be obvious is insufficient. Rather, one of ordinary skill in the art must have been motivated to select the references and to combine them. (See *Abbott Labs. v. Andrx Pharms., Inc.*, 452 F.3d 1331, 1336 (Fed.Cir.2006)). The cited references fail to provide this motivation.

Applicants would like to point out that although the Office Action correctly states that "the prior art does not teach chemically modifying the 2' positions of CpGs to reduce the non-specific effects triggered by such oligonucleotides..."; the Office Action goes on to state that nevertheless this would have been obvious because "the prior art, nevertheless, **clearly** taught that 2'-O-alkyl substitutions may be used to protect phosphorothioate oligonucleotides form nuclease-catalyzed degredation." (emphasis added) However, what is clear is that there is no connection between what the Office Action recognizes as Applicants patentable contribution and the teaching in the prior art relied upon to attempt to reject this contribution.

The best the Office Action can come up with is that since the prior teaches "that 2'-O-alkyl substitutions may be used to protect phosphorothioate oligonucleotides from nuclease-catalyzed degredation", and that "any C, G, A and/or T could be modified", then "**if** one or more 2'-O substitutions were incorporated into the C or G or both of a CG sequence in an oligo, the practitioner would expect to obtain the benefits disclosed by the prior art", but would also unknowingly obtain the properties discovered by Applicants. However, the standard for obviousness is not **if**. In order for there to be a prima facia case of obviousness there must be a teaching or suggestion within the prior art to motivate one skilled in the art to reach Applicants claimed invention.

The prior art clearly lacks this teaching. As recognized by the Office Action, the prior art does not teach chemically modifying the 2' positions of CpGs to reduce the non-specific effects triggered by such oligonucleotides. Furthermore, there is no teaching in the cited art recognizing the problem of CpG antisense oligonucleotides exhibiting toxic side effects (i.e., immune stimulation) or the use of 2'-O substitutions to solve this problem as taught by Applicants. Therefore, the use of 2'-O substitutions protect phosphorothioate oligonucleotides form nuclease-catalyzed degredation is not relevant (nor analogous) to a situation in which the compound is acting as a ligand to a receptor in an immunostimulatory pathway.

As the cited art does not provide the requisite teaching or suggestion to reach Applicants claimed invention, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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